REMARKS

Entry of the amendment is respectfully requested since it would either lessen the number of issues on appeal or result in the allowance of the application.

Claim 1, 3, 4, 7-8, and 10-13 are before the Examiner. Claim 1 has been amended to specify the manner of complex formation and claim 9 has been cancelled. The claim numbering reflects the action taken by the Examiner pursuant Rule 126.

Rejections under 35 USC 103

Claims 1-4 and 6-9 are rejected under 35 USC 103 as being unpatentable over Lowell et al. (V) or Smith et al. (W) or Averaham et al. (X) in view of Ratner et al. Applicants respectfully traverse.

Claim 1, as amended, describes an immunogenic composition comprising a proteosome-gp 160 complex and a pharmaceutically acceptable carrier where the complex is formed by a) lyopyhilizing a mixture of gp 160 and proteosomes, (b) dialysis of a mixture of gp 160 and proteosomes or c) by mixing gp 160 with proteosomes. Table 6 illustrates the impact of adjuvant (alum and SME) and protein types (GP 160, gp 41 and ALEX (gp 120)) on antibody production (ELISA). Claim 3, 4 and 13 high light the role of adjuvant in the context of gp 160. Note especially the results shown for SME (claim 13). Table 4 suggests complex preparation and proteosomes: peptide ratio impacts immunogenicity. Claims 10-12 highlight methods of preparation. Note especially the results shown for the method of claim 11.

The Examiner's position, as set for the in the Official Action, is that the general teaching provided in the primary references are applicable to any and all proteins or peptides and that it would be reasonable to expect that "improved" immunogenicity would result.

It is again submitted that the Smith et al. and Aversham et al. documents are silent as to the details of the technique(s) employed. The Lowell et al. article is also limited in this regard.

The instant specification clearly evidences variations in the degree of immunogenicity achieved by the different techniques and also with the variety of the peptide or protein treated. Note table 4 and the statement starting on line 19 of page 23. The Examiner general comments regarding the empirical nature of science is note. However, there is a higher degree of uncertainty in the immunological arts and weigh should be given to the positive results shown for gp 160.

It should be further noted gp160 is a transmembrane protein. It is much larger than the exemplified recombinant R32ft (a hydrophobic decapeptide). The specification treats them as distinct chemical entities. Gp160 forms trimers which results in "molecular complexes" having significantly larger molecular weights than the decapeptide. Even with this size, the immunogenicity of the trimeric complex is

enhanced with proteosomes and still more enhanced by the presence of adjuvants, such as alum, and also by the presence of submicron emulsions (SEM). This behavior is distinct from gp41 and Alex 10. See table 6 on page 40 of the instant specification. The Gp41 titers show a decrease from 680 to 565, when complexed with proteosomes, while gp160 titers increase from 30,274 to 51,112. Alex 10 titers decrease from 693 to 200 when submicron emulsions are substituted for alum, while gp160 increase from 51,112 to 104,644, with the same substitution. Clearly there is titer variation amongst the proteins and peptides, even those from the same source, not suggested by the art.

The differences associated with the gp160 titers are not expected from the references. As noted above the claims are not similarly situated relative to the teachings of the references. Clearly claim 1, as amended, is directed to an immunogenic composition having the complex having a limited ratio range of gp160 to proteosomes and where methods of complex preparation are specified. The complex is further characterized in terms of the effect of the adjuvant in terms of enhanced titer formation.

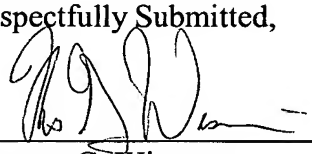
Even accepting the Examiner's premise as generally true, significant titer variation is shown between peptides and protein complexes and also in their manner of preparation. This variation is not expected from the applied art. Further, the degree of titer improvement for the disclosed gp160complex is not suggested and therefore is unexpected. These results mitigate against the sufficiency of the prima facie case.

For these reasons, withdrawal of the rejection is respectfully requested.

In view of the foregoing, reconsideration and allowance of this application are believed in order, and such action is earnestly solicited.

Dated: February 17, 2004

Respectfully Submitted,



Thomas G. Wiseman
Registration No. 35,046

VENABLE
P.O. Box 34385
Washington, D.C. 20043-9998
Telephone: (202) 344-4614
Telefax: (202) 344-8300

DC2-DOCS1-400389v2